REMARKS

Claims

The claims have not been amended relative to the Amendment filed May 22, 2007. Nevertheless, a claim listing is provided for the Examiner's convenience.

Rejection of Claims 1-3, 7, 18-22, 25 and 26 Under 35 U.S.C. § 112, First Paragraph

Claims 1-3, 7, 18-22, 25 and 26 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner states that she does not find support for a generic polymeric limitation with respect to carbohydrates. The Examiner further states that "[t]he specification appears to provide support only for those [carbohydrates] having some sort of branching and further comprising a saccharide moiety that interacts with a galectin."

The specification provides adequate support for the instant limitation. The specification at page 3, lines 11-13, states that "the materials of the present invention are generally comprised of natural or synthetic polymers and oligomers." Additional support can be found at page 5, lines 11-16: "preferred materials for the practice of the present invention generally comprise molecules which contain an active galectin binding sugar site, but which have somewhat higher molecular weights than simple sugars. Such molecules preferably have a minimum molecular weight of at least 300 daltons, and most typically a minimum molecular weight in the range of 300-2,000 daltons. Some specifically preferred materials have yet higher molecular weight ranges." While the latter passage does not explicitly reference carbohydrates with a polymeric backbone, one of ordinary skill in the art would recognize that polymeric backbones would be necessary for carbohydrates having these molecular weights. Moreover, the specification goes on to discuss a particular type of carbohydrate (i.e., a carbohydrate having a polymeric backbone with certain side chains) at page 5, lines 17-19. Thus, there is ample written description for the recitation of carbohydrates comprising a polymeric backbone. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Claims 1-4, 7 and 18-28 Under 35 U.S.C. § 103(a)

Claims 1-4, 7 and 18-28 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Klyosov *et al.* (US 6,645,946). Applicants previously submitted a Declaration Under 37 C.F.R. § 1.131, which the Examiner states is defective. Applicants submit herewith a new Declaration Under 37 C.F.R. § 1.131 ("Declaration"), which was been executed by Joseph Grimm, a representative of the Assignee of the entire interest, Prospect Therapeutics, Inc. As acknowledged by the Examiner, a petition under 37 C.F.R. § 1.47 was granted, so the Declaration may be signed by the 37 C.F.R. § 1.47 applicant or legal representative. Consideration of the newly-submitted Declaration is respectfully requested.

The experiments described in the Declaration are consistent with the recitations of the instant claims. Although Requester in the *inter partes* reexamination proceedings for the parent application (USSN 95/000,074) and Dr. Platt's counsel (as shown in Exhibit **1**, which was submitted with the Amendment of May 22, 2007) allege that interferon-2B is not a chemotherapeutic, Applicants have already fully rebutted these assertions in the reexamination proceedings. Moreover, Applicants have provided ample evidence that one of skill in the art would recognize interferon-2B as a chemotherapeutic.

In addition, the experiments described in the Declaration show that a carbohydrate having a polymeric backbone and which binds to a galectin enhances the efficacy of a chemotherapeutic. Although Requester in the reexamination proceedings and Dr. Platt's counsel allege that tumors in mice treated with interferon grew at a faster pace than tumors in the mouse control group, these assertions ignore the fact that the median days of survival were calculated ***excluding*** the mice that survived, such that this statistic alone is misleading regarding the success of the experiment. In fact, the Declaration demonstrates that the average tumor size in groups receiving both GBC590B, a carbohydrate that binds galectin, and interferon consistently lagged behind that of those receiving IFN or GBC-590 alone.

The Declaration establishes possession of the full scope of the claimed invention when taken in combination with the knowledge of a skilled artisan at the time. By the time of the study described in the Declaration, it was generally known in the art that modified pectin binds galectins, such as galectin-3, through its galactose residues and that other galectin-binding polymeric

carbohydrates would be expected to have similar biological activities. For example, an article by Platt (a co-inventor of the instant application) and Raz ("Modulation of the Lung Colonization of B16-F1 Melanoma Cells by Citrus Pectin," Journal of the National Cancer Institute, 84: 438-442 (1992), submitted as Exhibit **D** with the Declaration) discusses a prior study showing that galactoside-binding lectins have been shown to mediate cell-cell adhesion and cell-extracellular matrix adhesion through carbohydrates containing terminal galactosyl residues. Based upon this prior work, the article evaluates molecules rich in galactoside residues for modulating tumor cell colonization *in vivo*. In addition, U.S. Patent No. 5,834,442 (Exhibit **E**, submitted with the Declaration), filed July 7, 1994 and issued November 10, 1998, states that it had been previously demonstrated that modified citrus pectin could interfere with cell-cell interactions mediated by cell surface carbohydrate-binding galectin-3 molecules. This patent then teaches that complex carbohydrates rich in galactoside residues, such as pectin, act as potent inhibitors of prostate carcinoma metastasis. Furthermore, U.S. Patent No. 5,681,923 (Exhibit **F**, submitted with the Amendment of May 22, 2007), filed October 6, 1995 and issued October 28, 1997, for which co-inventor Platt is the sole inventor, discloses the sequence of galactose-specific binding polypeptides and the description of Figure 1 teaches that galactose bound to such polypeptides can be a simple sugar or a portion of a polysaccharide. Based on the inventors' knowledge of these facts and the results described in the Declarations, one of skill in the art would have reasonably expected that galectin-binding polymeric carbohydrates generally, particularly those containing terminal galactose moieties, would be useful in the claimed methods. It is particularly noteworthy that Platt, a co-inventor of the present invention, is also the co-author or the sole author of references demonstrating what a skilled artisan would have known as of the effective filing date of the instant application. Thus, the experiments described in the Declaration were sufficient, in conjunction with the knowledge of a skilled artisan and the specific knowledge of the inventors, to establish possession of the claimed invention.

Because Klyosov *et al.* is available as a reference only under 35 U.S.C. § 102(a) and/or (e), the Declaration antedates the reference and are effective to overcome the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-5, 7-9, 15-17, 20-23, 25, 26 and 28 Under 35 U.S.C. § 103(a)

Claims 1-5, 7-9, 15-17, 20-23, 25, 26 and 28 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Green *et al.* and Nangia-Makker *et al.* The Examiner states that it would have been obvious to one of ordinary skill in the art to modify the method of Green by substituting another agent such as modified citrus pectin. The Examiner further states that one of ordinary skill in the art would have had a reasonable expectation of success in this substitution.

Applicants respectfully disagree that one of ordinary skill in the art would have had a reasonable expectation in using a modified citrus pectin in the method of Green *et al*, as required by MPEP § 2143.02. In the instant case, Green *et al.* provide no teaching that a carbohydrate which binds to a galectin and comprises a polymeric backbone would be successful (or even useful) in their disclosed method. While Nangia-Makker *et al.* do employ modified citrus pectin and find that it can be used to neutralize endothelial cell morphogenesis, this *possible* anti-angiogenic effect in an *in vitro* culture is far removed from actually enhancing the efficacy of a chemotherapeutic in inhibiting tumor growth. As such, based upon the teachings of Green *et al.* and Nangia-Makker *et al.*, either separately or in combination, one of ordinary skill in the art would not have reasonably expected that administering a therapeutically effective amount of a carbohydrate which binds to a galectin and comprises a polymeric backbone *in vivo* would enhance the efficacy of a chemotherapeutic for inhibiting growth of a tumor in a patient. In order to make this extension of the references, it is necessary to further use the Applicants' own teachings of the effective *in vivo* enhancement. Of course, such use of Applicants' own teachings constitutes an impermissible application of hindsight reasoning. MPEP § 2142 ("The tendency to resort to "hindsight" based upon applicant"s disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.") Without a reasonable expectation of success, in light of which one of ordinary skill would likely not even have combined the cited references, the claimed method would not have been obvious. Reconsideration and withdrawal of the rejection are respectfully requested.

With respect to the declarations submitted with the Amendment filed May 22, 2007, Applicants note that synergy is not the standard for unexpected results. Instead, synergy is simply one type of unexpected result.

Rejection of Claims 18 and 19 Under 35 U.S.C. § 103(a)

Claims 18 and 19 are rejected as allegedly unpatentable over Green *et al.* and Nangia-Makker *et al.*, further in view of Raz *et al.* (US 5,834,442). The Examiner relies on Raz *et al.* for teaching particular routes of administration. Raz *et al.* do not cure the deficiencies of Green *et al.* and Nangia-Makker *et al.* discussed above because Raz *et al.* offer no teachings regarding the ability of carbohydrates containing a polymeric backbone and binding galectin to enhance the efficacy of a therapy for inhibiting tumor growth. Thus, for the same reasons as discussed above, the instant claims are not obvious over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 10-12 Under 35 U.S.C. § 103(a)

Claims 10-12 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Green *et al.* and Nangia-Makker *et al.*, further in view of Platt *et al.* (WO 97/34907), Ros *et al.* (Carbohydr. Res., 1996) and Renard *et al.* (Carbohyd. Res., 1995). The Examiner relies on Platt *et al.*, Ros *et al.* and Renard *et al.* for teaching the preparation of preparation of various pectins. Platt *et al.*, Ros *et al.* and Renard *et al.* do not cure the deficiencies of Green *et al.* and Nangia-Makker *et al.* discussed above because these references provide no teachings regarding the ability of carbohydrates containing a polymeric backbone and binding galectin to enhance the efficacy of a therapy for inhibiting tumor growth. Thus, for the same reasons as discussed above, the instant claims are not obvious over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance.

If a fee is due with this response, please charge our Deposit Account No. 18-1945, under Order No. 104831-0002-103 from which the undersigned is authorized to draw.

Dated: June 25, 2008

Respectfully submitted,

By _____

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